REMARKS

Reconsideration and allowance of this application are respectfully requested in light of the foregoing amendments and the following remarks.

Claim status

Claims 1 and 12 are amended. Claims 2-3, 8-9 and 13 are cancelled. Claims 1, 3-7, 10-12 and 14-18 are pending.

§103 Rejection

Claims 1, 4, 8-12 and 14-18 stand rejected as being unpatentable over U.S. Patent Application No. 2004/0045897 (hereinafter Nakabayashi) in view of U.S. Patent No. 4,765,987 (hereinafter Cadotte). Applicant respectfully traverses.

Applicant has amended claim 1 by incorporating claims 8 and 9 into its descriptions which now describes a method for production of an integrally asymmetric membrane with at least one separating layer and a supporting layer adjoining the separating layer, comprising the steps of: (a) preparation of a spinning solution comprising a membrane-forming polymer and a solvent system, the membrane forming polymer being a synthetic polymer selected from the group consisting of: polysulfones, polyphenylene sulfones, polyethersulfones, polyaryl ether sulfones, polyimides, polyetherimides, polycarbonates, polyetherketones and polyphenylene sulfides, or from the group of modifications of the cited polymers, or from the group of mixtures of the cited polymers, or from the group of copolymers of the monomers of the cited polymers;

(b) conversion of the spinning solution by means of a forming device into a shaped object with a first and a second surface; (c) preparing a precipitant system by dissolving a polyelectrolyte with negative fixed charges, but no positive fixed charges, into the precipitant system; (d) bringing of the first or second surface into contact with the precipitant system, wherein the precipitant system is such that formation of a membrane results in having a separating layer on the surface; the polyelectrolyte with negative fixed charges having a molecular weight of greater than 7000 daltons; wherein the polyelectrolyte with negative fixed charges is chosen from the group consisting of polysulfonic acids and polycarboxylic acids; wherein the polycarboxylic acids are partially cross-linked acrylic acids, copolymers of methacrylic acid and methyl methacrylate, copolymers of acrylic acid and vinylpyrrolidone, or copolymers of acrylic acid, vinylpyrrolidone and lauryl methacrylate; and (e) washing and, if necessary, drying of the membrane.

Applicant has also amended independent claim 12 to define an integrally asymmetric membrane with at least one separating layer and a supporting layer, characterised in that: the membrane is made from a synthetic polymer selected from the group consisting of; polysulfones, polyphenylene sulfones, polyethersulfones, polyaryl ether sulfones, polyimides, polyetherimides, polycarbonates, polyetherketones and polyphenylene sulfides, or from the group of modifications of the cited polymers, or from the group of mixtures of the cited polymers, or from the group of copolymers of the monomers of the cited polymers; and a polyelectrolyte with negative fixed charges, but having no positive fixed charges, is physically bound in the separating layer; the

polyelectrolyte with negative fixed charges having a molecular weight of greater than 7000 daltons; wherein the polyelectrolyte is chosen from the group consisting of polysulfonic acids and polycarboxylic acids, and wherein the polycarboxylic acids are partially cross-linked acrylic acids, copolymers of methacrylic acid and methyl methacrylate, copolymers of acrylic acid and vinylpyrrolidone, or copolymers of acrylic acid, vinylpyrrolidone and lauryl methacrylate; and characterised in that the supporting layer is free from polyelectrolyte

The Examiner claims that he has established a *prima facie* case of obviousness regarding claims 1 and 12 of the instant application. The MPEP § 2143 "Basic Requirements of a *Prima Facie* Case of Obviousness" states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine references teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.

Regarding the third criterion, the court has stated that "to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicant contends that in light of the amendments to claims 1 and 12 the prior art references Nakabayashi and Cadotte fail to teach, suggest, or provides a motivation for either a method for producing an integrally asymmetric membrane as described in the claim 1 of the instant invention or an integrally asymmetric membrane as described in the claim 12 of the instant invention.

The Examiner continues to rely on Nakabayashi in his refusal to allow independent claims 1 and 12. The Examiner admits that Nakabayashi is deficient in disclosing all of the elements required by claims 1 and 12. As Applicant has made clear on numerous occasions during the prosecution of the instant application, the Examiner's approach to reviewing the instant application is puzzling. Starting from Nakabayashi, it is not simply a question of functionalizing a membrane known in the art to simply improve the biocompatibility of a membrane (e.g. Scholander), improve the removal of ions by reverse osmosis membranes (Cadotte) or to selectively bind biomolecules to the membrane surface (Hou).

If Nakabayashi is taken as a starting point for determining inventive step, then the question arises as to how to improve the separation characteristics of the membranes of Nakabayashi, **not simply to functionalize the membrane for some unknown reason**. Improvement of the separation characteristics means to increase the separation efficiency, for example, between middle molecules, such as cytochrome c, and high-molecular proteins, such as albumin. (Specification, Page 3). As stated in previous responses, **none of the documents cited by the Examiner deals with separation characteristics of membranes**. The question which the Applicant must respectfully pose to the Examiner is simply why one skilled in the art should look to these documents if they fail to provide any hint or motivation regarding the improvement of separation characteristics of membranes. It is the Applicant's supposition that there is simply no other reasonable explanation except for impermissible hindsight

reconstruction to use, in particular, negatively charged polymeric groups from prior art cited by the Examiner in order to improve the separation characteristics of the membranes disclosed by Nakabayashi. The Examiner is arbitrarily picking elements from different documents and combining them in a manner that simply would not make logical sense to one having skill in the art who was attempting to arrive at the present invention.

In the instant office action, the Examiner believes that Nakabayashi discloses all of the elements of the above claims except for the inclusion of a polyelectrolyte with only negative fixed charges. Nakabayashi does not use a precipitant system comprising a polyelectrolyte having negative fixed charges, but instead uses a precipitant system in which a zwitterion is dissolved. However, when comparing the instant invention with Nakabayashi in the same manner as the Examiner, the relevant compounds, i.e. the polyelectrolyte having negative fixed charges in the instant invention and the zwitterion in Nakabayashi, are dissolved in the precipitant system. During the membrane manufacturing, the precipitant system is brought into contact with the spinning solution and interacts with the spinning solution in such a manner than the membrane polymer which was dissolved in the spinning solution precipitates out resulting in the formation of the membrane structure. Thus, when the spinning solution comes into contact with the precipitant system, and, hence, into contact with the polyelectrolyte and the zwitterion, respectively, the membrane as such is in statu nascendi.

The Examiner looks to Cadotte to make up for the deficiencies of Nakabayashi. Cadotte relates to reverse osmosis membranes having a crosslinked polyamide discriminating (separating) layer. According to Cadotte, instead of membranes in statu nascendi, readily prepared reverse osmosis membranes having polyamide separating layers are after-treated. Cadotte's membranes are after-treated with a strong mineral acid (Column 1, Lines 51-55) which may include polyphosphoric acid. The mineral acid must be strong enough to "modify the structure of the polyamide discriminating layer so as to increase the permeability to water. (Column 3, Line 65 – Column 4, Line 3). The concentration of these strong acids used by Cadotte is preferably from about 50 to about 85 weight percent (Column 4, Lines 9-12). Thus, Cadotte, in this respect, in no way deals with method for the production of membranes during which method the shaped membrane spinning solution is brought into contact with a precipitant system which comprises a polyelectrolyte with negative fixed charges. Additionally, Cadotte does not disclose anything regarding increasing the separation efficiency of a membrane. Instead, Cadotte discloses a method for increasing the water permeability of a readily prepared reverse osmosis membrane, while accepting a decrease in salt rejection which results from a simple treatment of the membrane with a strong acid which causes defects into the discriminating layer. (Column 5, Lines 23-25). Contrary to the Examiner's belief, the treatment of a readily prepared reverse osmosis membrane with a strong acid (e.g. polyphosphoric acid) as disclosed by Cadotte, does not functionalize the membrane, but simply changes the structure of the membrane.

Cadotte goes on to disclose a second step where the acid-treatment membranes are then treated with a rejection enhancing agent. Again, with respect to the rejection enhancing agents, Cadotte does not teach anything about functionalization of it membranes with these agents, but instead these agents simply alter the structure of the membranes in that they "selectively plug microscopic leaks and defects in the membrane discriminating layer. The preferred agents can even seal the porous support where discontinuities exist in the discriminating layer." (Column 5, Lines 35-40).

The rejection enhancing agents disclosed by Cadotte may be colloids. (Column 5, Lines 41-55). Another class of rejection enhancing agents includes water soluble polymers, one example mentioned by Cadotte being copolymers of hydroxyethyl methacrylate with methacrylic acid, the compound to which the Examiner refers to. However, in contrast to the Examiner's allegation, this compound is **not** a polyelectrolyte having a negative fixed charge, as required by claim 1 of the instant invention. According to claim 1 the polyelectrolyte with negative fixed charges may be a copolymer of methyl methacrylate and methacrylic acid which is different from a copolymer of hydroxyethyl methacrylate and methacrylic acid which is disclosed by Cadotte.

In summary, Cadotte first damages the discriminating layer with a strong acid and that damage simultaneously leads to both an increase in flux and to a decrease in rejection characteristic. Cadotte then attempts to repair the damages caused by the first step, to a certain extent, thereby bringing the rejection performance to a level

nearby, but still below the one of the untreated membrane. At the same time the flux is decreased to a level somewhat above the level of the untreated membrane. Thus, Cadotte in no way improves the separation efficiency of a membrane. There is only an improvement with respect to the flux, i.e. the permeability of the membranes (see Table I and Table III of Cadotte).

Thus, starting from Nakabayashi, there is simply no reason or motivation for one skilled in the art to look to Cadotte. Moreover, the teaching of Cadotte is of no help at all, if one skilled in the art is looking to improve the membranes of Nakabayashi with respect to an increase in separation efficiency. Additionally, Applicant has amended claim 1 by incorporating the hydrophobic polymers of claim 9 into its language and by deleting the inclusion of polyphosphoric acids from claim 1.

The prior art reference or combination of references relied upon by the Examiner must teach or suggest all of the limitations of the claims. See *In re Zurko*, 111 F.3d 887, 888-89, 42 U.S.P.Q.2d 1467, 1478 (Fed. Cir. 1997); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art."). The teachings or suggestions, as well as the expectation of success, must come from the prior art, not applicant's disclosure. See *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). In this instance, from the information detailed above, it is clear that both Nakabayashi and Cadotte fail to teach or suggest all the limitations of Applicant's claims. Accordingly, neither Nakabayashi nor Cadotte disclose all of the elements of

claims 1 or 12 and therefore, this rejection must fail. Thus, claims 1 and 12 are not obvious over Nakabayashi in view of Cadotte and should be allowed.

In reference to claims 4, 10-11 and 14-18, dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious. *Hartness Int'l, Inc. v. Simplimatic Eng'g Co., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987); In re Abele, 684 F.2d 902, 910, 214 USPQ 682, 689 (CCPA 1982); see also In re Semaker, 702 F.2d 989, 991, 217 USPQ 1, 3 (Fed. Cir. 1983).* Thus, claims 4, 10-11 and 14-18 are not obvious over Nakabayashi in view of Cadotte and should be allowed.

Claims 1, 4-12 and 14-18 stand rejected as being unpatentable over EP No. 0568045 (hereinafter Kawata) in view of WO No. 00/50160 (hereinafter Hou). Applicant respectfully traverses.

Again, the Examiner claims that he has established a *prima facie* case of obviousness regarding claims 1 and 12 of the instant application. The MPEP § 2143 "Basic Requirements of a *Prima Facie* Case of Obviousness" states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine references teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.

Regarding the third criterion, the court has stated that "to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicant contends that in light of the amendments to claims 1 and 12 the prior art references Kawata and Hou fail to teach, suggest, or provides a motivation for either a method for producing an integrally asymmetric membrane as described in the claim 1 of the instant invention or an integrally asymmetric membrane as described in the claim 12 of the instant invention.

The Examiner alleges that claims 1, 4, 12 and 14-1 are unpatentable over Kawata in view of Hou. He argues that Kawata discloses a method for producing asymmetric membranes in which process (1) a spinning solution is prepared comprising a membrane forming polymer and a solvent system and (2) the spinning solution is converted into a shaped object with a first and a second surface. The Examiner then alleges that the first and/or second surface is brought into contact with a precipitating system comprising a polyelectrolyte with negative fixed charges but no positive charges, referring specifically to claims 6 and 8 of Kawata.

With all respect due to the Examiner, Applicant must point out that nowhere in claims 6 and 8 and nowhere in the specification of Kawata is there disclosed a polyelectrolyte with negative fixed charges. Kawata discloses a process for manufacturing hollow fiber membranes, in which process use is made of vinylpyrrolidone-based polymers in the polymer solution and in the inner coagulation

liquid. The aim of Kawata is to provide a membrane having improved biocompatibility and a water-permeability that does not deteriorate after drying (Page 41, Lines 30-33). Kawata achieves this with a membrane having the vinylpyrrolidone based polymer within the membrane wall with an increased concentration of the polymer in the inner skin layer (See claim 1). One of the vinylpyrrolidone polymers disclosed by Kawata and specifically referred to by the Examiner is a copolymer of vinylpyrrolidone and dimethylaminoethyl methacrylate.

However, the Examiner is simply incorrect in saying that Kawata discloses bringing the first and/or second surface into contact with a precipitating system comprising a polyelectrolyte with negative fixed charges but no positive charges. One having skill in the art would know that none of the vinylpyrrolidone-based polymers disclosed by Kawata is a polyelectrolyte with negative fixed charges. Every organic chemist would recognize that the vinylpyrrolidone-based polymers disclosed by Kawata **have no charge**. This is true in particular with respect to the copolymer of vinylpyrrolidone and dimethylaminoethyl methacrylate relied upon by the Examiner.

Thus, according to the Examiner, starting from Kawata, the object of the present invention is to provide a membrane having improved separation characteristics. This objective is achieved by bringing the first and/or second surface into contact with a precipitating system comprising a polyelectrolyte with negative fixed charges but no positive charges. However, there is no hint in Kawata regarding improvement of the separation characteristics. Kawata simply does not deal with the improvement of

separation characteristics, but instead deals with improvements of biocompatibility. Moreover, there is absolutely no hint in Kawata regarding the use of polyelectrolytes, let alone polyelectrolytes with negative fixed charges.

Regarding this substantial deficiency, Hou offers no aid to Kawata. As explained in a previous response, Hou relates to negatively charged microporous membranes comprising a porous substrate and a crosslinked coating (Page 1, Lines 10-13) and a process for preparing these membranes (Page 11, Line16, to Page 12, Line 4). In the process of Hou, a readily prepared porous substrate is used. This porous substrate can be made, for example, by a phase inversion process and can be a membrane. (Page 9, Line 29 to Page 10, Line 3). From the description of Hou, it becomes evident that the porous substrate is a pre-fabricated substrate which is coated with a coating solution after fabrication. Hou aims at selectively binding biomolecules to the membrane (Page 1, Lines 24-27) by applying a specific crosslinked coating to the prefabricated substrate. Hou clearly does not relate to improvement of the separation efficiency of the membrane regarding compounds differing in size as required by the instant invention. (See Specification, Page 2, Paragraph 2; Page 3, last paragraph).

The negative charge of the microporous membranes of Hou is effected by a crosslinked coating having pendant anionic groups. As can be seen from claim 2 of Hou, the crosslinked coating is prepared from a polymerized composition comprising an unsaturated monomer having an anionic group, at least one or more N-(hydroxyalky1)-

or N-(alkoxyalky1)-acrylamide and a hydrophilic unsaturated monomer. Thus, the anionic groups are provided by the unsaturated monomer having an anionic group.

According to claim 18 of Hou (referred to by the Examiner), the composition used to prepare the crosslinked coating may include in addition a further acrylic monomer having a carboxylic acid group which is copolymerized into the crosslinked coating. Applicant must specifically point out to the Examiner that the crosslinking of the composition to form the coating would, after the crosslinking reaction, in no case lead to a polyelectrolyte with negative fixed charges as required by claim 1 of the instant invention. **The chemical structure is simply and clearly different!**

The Examiner now alleges that it would have been obvious to one having ordinary skill in the art to modify the method of Kawata to include acrylic acid in the polyelectrolyte solution as taught by Hou. However, claim 1 of the instant invention does not allow just any acrylic acid to be added to the precipitation system, but only the specific carboxylic acids listed in claim 1, which are partially crosslinked acrylic acids, copolymers of methacrylic acid and methyl methacrylate, copolymers of acrylic acid and vinylpyrrolidone and copolymers of acrylic acid, vinylpyrrolidone and lauryl methacrylate. The Examiner's reliance on Hou is simply misplaced as these compounds are clearly not disclosed in Hou.

As mentioned above, Kawata does not deal with improvement of membrane separation characteristics but with improvement of membrane biocompatibility. There is

no hint in Kawata regarding use of polyelectrolytes, let alone of polyelectrolytes with negative fixed charges.

Therefore, the question already arises whether Kawata can serve as a relevant prior art for the one skilled in the art who wants to have a membrane with improved separation efficiency. One having skill in the art would know that there is simply no starting point in Kawata with respect to separation efficiency.

However, if nevertheless the one skilled in the art takes Kawata as a starting point, why should he or she exchange the (uncharged) vinylpyrrolidone-based polymers used by Kawata and switch to a precipitant system comprising polymers with fixed charges?

Why should he or she use polyelectrolytes with negative fixed charges (and not polyelectrolytes with positive fixed charges?

Why should one skilled in the art take a look at Hou and take one reacting agent from a composition which is chemically crosslinked into a coating on a membrane, this coating being applied to a readily prepared membrane in order to improve selectively binding of biomolecules to the membrane. Why should he or she do this if they want to improve the separation characteristics of the membranes of Kawata.

Moreover, why should they put this reacting agent, which is used by Hou in a composition for making a crosslinked coating to be applied in an after-treatment process step onto a membrane, instead into a precipitant system used in a manufacturing process of a membrane, which precipitant system is brought into contact with a membrane spinning solution in order to precipitate the membrane polymer in the spinning solution to form the membrane structure.

There is no reason at all for one skilled in the art nor motivation for such a procedure. The argumentation of the Examiner is based on hindsight view. The Examiner collects elements from different origins not being connected to each other and combines these elements in an arbitrary way. Such an approach, however, is inadmissible. The Examiner's reliance on Kawata and Hou appears to be either a misreading of Kawata and Hou, a misinterpretation of Kawata and Hou, or an ex post facto analysis of Kawata and Hou which amounts to impermissible hindsight reconstruction.

Hindsight reconstruction is not permitted as the Federal Circuit has repeatedly warned that the requisite motivation to modify a reference must come from the prior art, not Applicant's specification. See *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988) ("there must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure.") Using an Applicant's disclosure as a blueprint to reconstruct the claimed invention from isolated piece of the prior art contravenes the statutory

mandate of section 103 of judging obviousness at the point in time when the invention was made. See *Grain Processing Corp. v. American Maize-Prods. Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988).

Only hindsight reconstruction based upon the instant specification would lead the Examiner to the conclusion that the claims in the instant application are rejected under §103 as unpatentable over Kawata in view of Hou. Accordingly, the instant rejection must be removed.

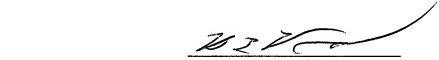
The prior art reference or combination of references relied upon by the Examiner must teach or suggest all of the limitations of the claims. See *In re Zurko*, 111 F.3d 887, 888-89, 42 U.S.P.Q.2d 1467, 1478 (Fed. Cir. 1997); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art."). The teachings or suggestions, as well as the expectation of success, must come from the prior art, not applicant's disclosure. See *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). In this instance, from the information detailed above, it is clear that both Kawata and Hou fail to teach or suggest all the limitations of Applicant's claims. Accordingly, neither Kawata nor Hou disclose all of the elements of claims 1 or 12 and therefore, this rejection must fail. Thus, claims 1 and 12 are not obvious over Kawata in view of Hou and should be allowed.

In reference to claims 4-11 and 14-18, dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious. *Hartness Int'l, Inc. v. Simplimatic Eng'g Co., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987); In re Abele, 684 F.2d 902, 910, 214 USPQ 682, 689 (CCPA 1982); see also In re Sernaker, 702 F.2d 989, 991, 217 USPQ 1, 3 (Fed. Cir. 1983).* Thus, claims 4-11 and 14-18 are not obvious over Kawata in view of Hou and should be allowed.

Conclusion

In view of the foregoing, Applicant respectfully requests an early Notice of Allowance in this application.

Respectfully submitted,



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